L10 ANSWER 8 OF 24 MEDLINE
AN 95157182 MEDLINE
DN 95157182 PubMed ID: 7854056
TI Expression of the growth-associated protein B-50/GAP43 via a defective herpes-simplex virus vector results in profound morphological changes in **non-neuronal** cells.
AU Verhaagen J; Hermens W T; Oestreicher A B; Gispen W H; Rabkin S D; Pfaff D W; Kaplitt M G
CS Rudolf Magnus Institute, Department of Medical Pharmacology, Utrecht, The Netherlands.
SO BRAIN RESEARCH. MOLECULAR BRAIN RESEARCH, (1994 Oct) 26 (1-2) 26-36. Journal code: MBR; 8908640. ISSN: 0169-328X.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199503
ED Entered STN: 19950322
Last Updated on STN: 19980206
Entered Medline: 19950316
AB This study describes the creation and application of a defective herpes simplex viral (HSV) vector for B-50/GAP-43, a neural growth-associated phosphoprotein. We demonstrate abundant expression of B-50/GAP-43 in cultured **non-neuronal** cells (African green monkey kidney cells [vero cells] and Rabbit skin cells) via this HSV vector. When B-50/GAP-43 was expressed in **non-neuronal** cells major morphological changes occurred that included **extensive** membrane ruffling, the formation of filopodia and long thin **extensions** reminiscent of neurites. These **extensions** often terminated in **growth cone**-like structures. Quantitation of these morphological changes at different times following infection demonstrates that the surface area of the B-50/GAP-43-expressing cells started to increase between 6 and 10 h post-infection. At 72 h, B-50/GAP-43-positive cells were 3.0 times larger in size and one third of the cells expressed long processes with a mean length of 165 +/- 14.5 microns. Ultrastructural studies of cells 48 h after infection revealed that B-50/GAP-43 is predominantly localized at the plasma membrane of the elaborated processes. Some immunoreactivity was associated with vesicular structures that appear to be in-transit in the processes. These observations suggest that B-50/GAP-43 acts at the plasmamembrane to induce a neuron-like morphology in **non-neuronal** cells persisting for several days in culture. In the future the defective viral vector will enable gene transfer to express B-50/GAP-43 in neurons in vivo in order to study its involvement in regenerative sprouting and neuroplasticity.

L10 ANSWER 10 OF 24 MEDLINE
AN 94230600 MEDLINE
DN 94230600 PubMed ID: 8175908
TI An amino-terminal domain of the growth-associated protein GAP-43 mediates its effects on filopodial formation and cell spreading.
AU Strittmatter S M; Valenzuela D; Fishman M C
CS Developmental Biology Laboratory, Massachusetts General Hospital, Charlestown.
SO JOURNAL OF CELL SCIENCE, (1994 Jan) 107 (Pt 1) 195-204.
Journal code: HNK; 0052457. ISSN: 0021-9533.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199406
ED Entered STN: 19940620
Last Updated on STN: 19980206
Entered Medline: 19940606
AB GAP-43 is a neuronal protein that is believed to be important to neuronal growth and nerve terminal plasticity. It is enriched on the inner surface of **growth cone** membranes, a localization that may depend upon palmitoylation of Cys3 and Cys4. It is a major substrate for protein kinase C, which phosphorylates Ser41. Isolated GAP-43 can bind to actin and to calmodulin, and can activate the heterotrimeric GTP-binding proteins, G(o) and Gi. A peptide consisting of the GAP-43 sequence 39-55 binds calmodulin, and an amino-terminal GAP-43 (1-10) peptide activates G(o), suggesting that these stretches may be functional domains of the intact protein. When expressed in **non-neuronal** cells, GAP-43 enhances filopodial **extension** and has effects upon cell spreading. We have examined the effects of various GAP-43 domains upon this assay, by expression of GAP-43, GAP-43 mutant proteins, and GAP-43-CAT fusion proteins in COS-7 cells. We find that the amino terminus (Met-Leu-Cys-Cys-Met-Arg-Arg-Thr-Lys-Gln) is an important contributor to these effects on cell shape. A GAP-43 protein mutant in Cys3 and Cys4 does not bind to the membrane, and is inactive. Mutants in Arg6 or Lys9 also are inactive, although they remain localized to particulate fractions; Arg7 mutants are active. A chimeric gene consisting of GAP-43 (1-10) fused to chloramphenicol acetyl transferase (CAT) also causes cell shape changes. As for GAP-43, the effects of this fusion protein are abolished by mutations of Cys3, Cys4, Arg6 or Lys9, but not by mutation of Arg7. Therefore, the cell surface activity of transfected GAP-43 depends upon its amino terminus, although other domains may regulate it in this regard.
Since the amino-terminal domain includes the peptide stretch known to be capable of activating G(o) and Gi, we examined the effect of GAP-43 on a Gi-regulated second messenger system, the inhibition of cAMP production in A431 cells. A431 cells stably transfected with GAP-43 spread less well than do controls. In addition, they evidence decreased levels of forskolin-stimulated cAMP, consistent with chronic stimulation of Gi. Stimulation of adenylate cyclase by isoproterenol reverses the GAP-43-induced changes in cell shape. This suggests that G protein stimulation is involved in GAP-43 effects upon cell shape.

L14 ANSWER 1 OF 174 MEDLINE
AN 1999028889 MEDLINE
DN 99028889 PubMed ID: 9812346
TI Effect of sublethal doses of cadmium, inorganic mercury and methylmercury on the cell morphology of an insect cell line (Aedes albopictus, C6/36).
AU Braeckman B; Simoens C; Rzeznik U; Raes H
CS Department of Biochemistry, Physiology and Microbiology, University of Gent, Belgium.
SO CELL BIOLOGY INTERNATIONAL, **(1997 Dec)** 21 (12) 823-32.
Journal code: BPN; 9307129. ISSN: 1065-6995.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199812
ED Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981201
AB The effect of CdCl2 (44 microM), HgCl2 (3.7 microM), and MeHgCl (2 microM)
on the morphology of Aedes albopictus C6/36 cells was studied at the light
microscopical level. Treatment times and metal concentrations were in the sublethal range as determined by a fluorometric dye exclusion test. The three metal species had profound effects on the cell morphology. MeHgCl treatment induced the development of a large number of short, actin-supported, tangled **filopodia**. Both CdCl2 and HgCl2 induced long **extensions**. Pretreatment with colchicine but not with cytochalasin B prevented formation of these **extensions** which suggests that they were supported by microtubules. This was confirmed by immunostaining for microtubules. The extensions were relatively stable towards colchicine post-treatment. To authors' knowledge, this effect has not yet been described for heavy metals. The similarity with 20-hydroxyecdysone-treated cells and the occurrence of cytoplasmic feet in
insect cells is discussed.

L14 ANSWER 4 OF 174 MEDLINE
AN 1998028160 MEDLINE
DN 98028160 PubMed ID: 9362067
TI Integrin alpha 6A beta 1 induces CD81-dependent cell motility without engaging the extracellular matrix migration substrate.
AU Domanico S Z; Pelletier A J; Havran W L; Quaranta V
CS Department of Cell Biology, Scripps Research Institute, La Jolla, California 92037, USA.
NC CA-47858 (NCI)
DE-10063 (NIDCR)
SO MOLECULAR BIOLOGY OF THE CELL, **(1997 Nov)** 8 (11) 2253-65.
Journal code: BAU; 9201390. ISSN: 1059-1524.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199712
ED Entered STN: 19980109
Last Updated on STN: 20000303
Entered Medline: 19971211
AB It is well established that integrins and extracellular matrix (ECM) play key roles in cell migration, but the underlying mechanisms are poorly defined. We describe a novel mechanism whereby the integrin alpha 6 beta 1, a laminin receptor, can affect cell motility and induce migration onto ECM substrates with which it is not engaged. By using DNA-mediated gene transfer, we expressed the human integrin subunit alpha 6A in murine embryonic stem (ES) cells. ES cells expressing alpha 6A (ES6A) at the surface dimerized with endogenous beta 1, **extended** numerous **filopodia** and lamellipodia, and were intensely migratory in haptotactic assays on laminin (LN)-1. Transfected alpha 6A was responsible for these effects, because cells transfected with control vector or alpha 6B, a cytoplasmic domain alpha 6 isoform, displayed compact morphology and no migration, like wild-type ES cells. The ES6A migratory phenotype persisted on fibronectin (Fn) and Ln-5. Adhesion inhibition assays indicated that alpha 6 beta 1 did not contribute detectably to adhesion to these substrates in ES cells. However, anti-alpha 6 antibodies completely blocked migration of ES6A cells on Fn or Ln-5. Control experiments with monensin and anti-ECM antibodies indicated that this inhibition could not be explained by deposition of an alpha 6 beta 1 ligand (e.g., Ln-1) by ES cells. Cross-linking with secondary antibody overcame the inhibitory effect of anti-alpha 6 antibodies, restoring migration or **filopodia extension** on Fn and Ln-5. Thus, to induce migration in ES cells, alpha 6A beta 1 did not have to engage with an ECM ligand but likely participated in molecular interactions sensitive to anti-alpha 6 beta 1 antibody and mimicked by cross-linking. Antibodies to the tetraspanin CD81 inhibited alpha 6A beta 1-induced migration but had no effect on ES cell adhesion. It is known that CD81 is physically associated with alpha 6 beta 1, therefore our results suggest a mechanism by which interactions between alpha 6A beta 1 and CD81 may up-regulate cell motility, affecting migration mediated by other integrins.

L14 ANSWER 5 OF 174 MEDLINE
AN 97412181 MEDLINE
DN 97412181 PubMed ID: 9265651
TI PSTPIP: a tyrosine phosphorylated cleavage furrow-associated protein that is a substrate for a PEST tyrosine phosphatase.

AU Spencer S; Dowbenko D; Cheng J; Li W; Brush J; Utzig S; Simanis V; Lasky L
A
CS Department of Molecular Oncology, Genentech, Inc., South San Francisco, California 94080, USA.
SO JOURNAL OF CELL BIOLOGY, **(1997 Aug 25)** 138 (4) 845-60.
Journal code: HMV; 0375356. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U87814
EM 199709
ED Entered STN: 19970926
Last Updated on STN: 19990129
Entered Medline: 19970915
AB We have investigated proteins which interact with the PEST-type protein tyrosine phosphatase, PTP hematopoietic stem cell fraction (HSCF), using the yeast two-hybrid system. This resulted in the identification of proline, serine, threonine phosphatase interacting protein (PSTPIP), a novel member of the actin- associated protein family that is homologous to
Schizosaccharomyces pombe CDC15p, a phosphorylated protein involved with the assembly of the actin ring in the cytokinetic cleavage furrow. The binding of PTP HSCF to PSTPIP was induced by a novel interaction between the putative coiled-coil region of PSTPIP and the COOH-terminal, proline-rich region of the phosphatase. PSTPIP is tyrosine phosphorylated both endogenously and in v-Src transfected COS cells, and cotransfection of dominant-negative PTP HSCF results in hyperphosphorylation of PSTPIP. This dominant-negative effect is dependent upon the inclusion of the COOH-terminal, proline-rich PSTPIP-binding region of the phosphatase. Confocal microscopy analysis of endogenous PSTPIP revealed colocalization with the cortical actin cytoskeleton, lamellipodia, and actin-rich cytokinetic cleavage furrow. Overexpression of PSTPIP in 3T3 cells resulted in the formation of **extended filopodia,** consistent with a role for this protein in actin reorganization. Finally, overexpression of mammalian PSTPIP in exponentially growing S. pombe results in a dominant-negative inhibition of cytokinesis. PSTPIP is therefore a novel actin-associated protein, potentially involved with cytokinesis, whose tyrosine phosphorylation is regulated by PTP HSCF.

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L14 ANSWER 2 OF 174 MEDLINE
AN 1998075097 MEDLINE
DN 98075097 PubMed ID: 9412479
TI The integrin alpha6beta4 functions in carcinoma cell migration on laminin-1 by mediating the formation and stabilization of actin-containing motility structures.
AU Rabinovitz I; Mercurio A M
CS Department of Medicine (GI Division), Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts 02215, USA.
NC AI39264 (NIAID)
CA44704 (NCI)
SO JOURNAL OF CELL BIOLOGY, **(1997 Dec 29)** 139 (7) 1873-84.
Journal code: HMV; 0375356. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199802
ED Entered STN: 19980217
Last Updated on STN: 20000303
Entered Medline: 19980205
AB Functional studies on the alpha6beta4 integrin have focused primarily on its role in the organization of hemidesmosomes, stable adhesive structures that associate with the intermediate filament cytoskeleton. In this study, we examined the function of the alpha6beta4 integrin in clone A cells, a colon carcinoma cell line that expresses alpha6beta4 but no alpha6beta1 integrin and exhibits dynamic adhesion and motility on laminin-1. Time-lapse videomicroscopy of clone A cells on laminin-1 revealed that their migration is characterized by **filopodial extension** and stabilization followed by lamellae that **extend** in the direction of stabilized **filopodia**. A function-blocking mAb specific for the alpha6beta4 integrin inhibited clone A migration on laminin-1. This mAb also inhibited filopodial formation and stabilization and lamella formation. Indirect immunofluorescence microscopy revealed that the alpha6beta4 integrin is localized as discrete clusters in filopodia, lamellae, and retraction fibers. Although beta1 integrins were also localized in the same structures, a spatial separation of these two integrin populations was evident. In filopodia and lamellae, a striking colocalization of the alpha6beta4 integrin and F-actin was seen. An association between alpha6beta4 and F-actin is supported by the fact that alpha6beta4 integrin and actin were released from clone A cells by treatment with the F-actin- severing protein gelsolin and that alpha6beta4 immunostaining at the marginal edges of clone A cells on laminin-1 was resistant to solubilization with Triton X-100. Cytokeratins were not observed in filopodia and lamellipodia. Moreover, alpha6beta4 was extracted from these marginal edges with a Tween-40/deoxycholate buffer that solubilizes the actin cytoskeleton but not cytokeratins. Three other carcinoma cell lines (MIP-101, CCL-228, and MDA-MB-231) exhibited alpha6beta4 colocalized with actin in filopodia and lamellae. Formation of lamellae in these cells was inhibited with an alpha6-specific antibody. Together, these results indicate that the alpha6beta4 integrin functions in carcinoma migration on laminin-1 through its ability to promote the formation and stabilization of actin-containing motility structures.

L2 ANSWER 1 OF 1 MEDLINE
AN 1999223289 MEDLINE
DN 99223289 PubMed ID: 10208590
TI **Isolation** of **human delta-catenin** and its binding specificity with presenilin 1.
AU Tanahashi H; Tabira T
CS Division of Demyelinating Disease and Aging, National Institute of Neuroscience, Kodaira, Tokyo, Japan.
SO NEUROREPORT, (1999 Feb 25) 10 (3) 563-8.
Journal code: 9100935. ISSN: 0959-4965.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AB013805
EM 199906
ED Entered STN: 19990618
Last Updated on STN: 19990618
Entered Medline: 19990610
AB We screened proteins for interaction with presenilin (PS) 1, and cloned the full-length cDNA of human delta-catenin, which encoded 1225 amino acids. Yeast two-hybrid assay, GST binding assay and immunoprecipitation demonstrated that delta-catenin interacted with a hydrophilic loop region in the endoproteolytic C-terminal fragment of PS1, but not with that of PS-2. These results suggest that PS1 and PS2 partly differ in function. PS1 loop fragment containing the pathogenic mutation retained the binding ability. We also found another armadillo-protein, p0071, interacted with PS1.